

NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

SMITHKLINE BEECHAM CORPORATION:

d/b/a GLAXOSMITHKLINE,

:

Plaintiff,

:

Civil Action No. 02-3779(JWB)

v.

:

O P I N I O N

TEVA PHARMACEUTICALS USA, INC.,

:

Defendant.

:

APPEARANCES:

DRINKER BIDDLE & REATH

By: John J. Francis, Jr., Esquire

500 Campus Drive

Florham Park, New Jersey 07932-1047

- and -

FITZPATRICK, CELLA, HARPER & SCINTO

By: Nicholas M. Cannella, Esquire

30 Rockefeller Plaza

New York, New York 10112

(Attorneys for Plaintiff)

WOLF, BLOCK, SCHORR and SOLIS-COHEN

By: Robert J. Fettweis, Esquire

744 Broad Street

Newark, New Jersey 07102

- and -

KENYON & KENYON

By: James Galbraith, Esquire

Steven J. Lee, Esquire

One Broadway

New York, New York 10004

(Attorneys for Defendant)

BISSELL, Chief Judge

This matter comes before the Court on a motion by Plaintiff Smithkline Beecham Corp. ("SKB") for summary judgment of no inequitable conduct in the prosecution of the patent-in-suit. The Court heard oral arguments on the instant motion on May 10, 2004. The Court has jurisdiction over this case pursuant to 28 U.S.C. § 1338.

FACTS AND BACKGROUND¹

Plaintiff filed a patent infringement suit to protect its rights under U.S. Patent 4,602,017 (the "'017 patent") which is sold by plaintiff under the trade name Lamictal®. The '017 patent covers inter alia, lamotrigine, pharmaceutical compositions containing lamotrigine and methods of using lamotrigine to treat convulsions in mammals and epilepsy in humans. Pl. Br. at 2. Defendant Teva Pharmaceuticals USA, Inc. ("Teva") filed Abbreviated New Drug Applications ("ANDA") with the Food and Drug Administration ("FDA") seeking approval to market generic versions of the '017 patent. Teva alleged in its Paragraph IV certification² that every claim except claim 5 of

¹ A complete recitation of the facts of this case can be found in this Court's March 5, 2003 Opinion. In this Opinion, the Court will include those general facts which are also relevant to the instant motion.

² The ANDA must include a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV certification") stating that the patent is invalid and/or will not be infringed by the generic version. In addition to filing an ANDA and a

the '017 patent is either invalid or would not be infringed by the commercial manufacture, use or sale of the product covered in the ANDAs.³ Teva alleged, inter alia, that the '017 patent was invalid because SKB engaged in inequitable conduct. After receiving Teva's Paragraph IV notices, SKB timely filed separate infringement actions against Teva. The cases were consolidated by this Court on November 27, 2002.

DISCUSSION

I. Standard for Summary Judgment

Federal Rule of Civil Procedure 56(c) provides that summary judgment should be granted "if the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." Fed. R. Civ. P. 56(c); see also Chipollini v. Spencer Gifts, Inc., 814 F.2d 893, 896 (3d Cir. 1987) (en banc), cert. dismissed, 483 U.S. 1052 (1987). In deciding a motion for summary judgment, a court must view the facts in the light most favorable to the nonmoving party and must

Paragraph IV certification, the generic manufacturer must give notice of the ANDA and Paragraph IV certification to the patent holder. 21 U.S.C. § 355 (j)(2)(B)(i).

³ Teva sought to market generic versions of SKB's lamotrigine tablets and lamotrigine chewable dispersible tablets. The ANDAs did not cover the injectable solution containing lamotrigine.

resolve any reasonable doubt as to the existence of a genuine issue of fact against the moving party. Continental Ins. Co. v. Bodie, 692 F.2d 436, 438 (3d Cir. 1982). The moving party has the burden of establishing that there are no genuine issues of material fact. Celotex Corp. v. Catrett, 477 U.S. 317, 322-24 (1986).

The Supreme Court has stated that, in applying the criteria for granting summary judgment:

the judge must ask ... not whether ... the evidence unmistakably favors one side or the other but whether a fair-minded jury could return a verdict for the [nonmoving party] on the evidence presented. The mere existence of a scintilla of evidence in support of the [non-movant's] position will be insufficient; there must be evidence on which the jury could reasonably find for the [nonmoving party]. The judge's inquiry, therefore, unavoidably asks whether reasonable jurors could find by a preponderance of the evidence that the [non-movant] is entitled to a verdict.

Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 252 (1986). A fact is "material" only if it will affect the outcome of a lawsuit under the applicable law, and a dispute over a material fact is "genuine" if the evidence is such that a reasonable factfinder could return a verdict for the nonmoving party. Id.

II. Standard and Burden of Proof
for Claims of Inequitable Conduct

A party attempting to prove inequitable conduct must have evidence of "affirmative misrepresentations of a material fact,

failure to disclose material information or submission of false material information, coupled with an intent to deceive." Dayco Prods., Inc. v. Total Containment, Inc., 329 F.3d 1358, 1362 (Fed.Cir. 2003) (quoting Purdue Pharma L.P. v. Boehringer Ingelheim GMBH, 237 F.3d 1359, 1366 (Fed. Cir. 2001)). Intent and materiality are questions of fact that must be proven by clear and convincing evidence. Id. Once the threshold requirements for these factual inquiries are met, "those fact findings are balanced to make the determination whether 'the scales tilt to a conclusion that inequitable conduct occurred.'" Manville Sales Corp. v. Paramount Sys., Inc., 917 F.2d 544, 551 (Fed. Cir. 1990). "[T]he more material the omission or the misrepresentation, the lower the level of intent required to establish inequitable conduct, and vice versa." Monon Corp. v. Stoughton Trailers, Inc., 239 F.3d 1253, 1261 (Fed. Cir. 2001) (quoting Critikon, Inc. v. Becton Dickinson Vascular Access, Inc., 120 F.3d 1253, 1256 (Fed. Cir. 1997)). In order to survive a motion for summary judgment of no inequitable conduct, the non-movant must offer evidence or legal argument whereby, when drawing all factual inferences in its favor, the clear and convincing standard of proof would be met at trial. See Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565, 1583 (Fed. Cir. 1991).

A. Materiality

37 C.F.R. § 1.56(a)(1991) defined materiality using a "reasonable examiner" standard. It provided:

A duty of candor and good faith toward the Patent and Trademark Office rests on the inventor, on each attorney or agent who prepares or prosecutes the application and on every other individual who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee or with anyone to whom there is an obligation to assign the application. All such individuals have a duty to disclose to the Office information they are aware of which is material to the examination of the application. Such information is material where there is a substantial likelihood that a reasonable examiner would consider it important in deciding whether to allow the application to issue as a patent.

37 C.F.R. § 1.56(a)(1991).⁴

An analysis of materiality cannot be done in a vacuum as it is "not dependent on a single element viewed in isolation." Baxter Int'l Inc. v. McGaw, Inc., 149 F.3d 1321, 1328 (Fed. Cir. 1998).

"Rather, it is judged based upon the overall degree of similarity between the omitted reference and the claimed invention in light of the other prior art before the examiner." Id. at 1328.

1. Non-Disclosure of the Reynolds References

⁴ In 1992, the Patent and Trademark Office ("PTO") amended its rule to provide a different standard for materiality. "The new rule reiterated the preexisting duty of 'candor and good faith', but more narrowly defined materiality, providing for disclosure where the information establishes either 'a prima facie case of unpatentability' or 'refutes, or is inconsistent with a position the applicant takes'." Dayco Products, 329 F.3d at 1363-64. The Federal Circuit has continued to apply the reasonable examiner standard to cases that were prosecuted under the earlier version of Rule 56. Id. at 1364. Therefore, because the '017 patent was prosecuted before the PTO in 1979, the reasonable examiner standard will apply in the instant action.

Teva alleges that SKB should have disclosed to the PTO, during the prosecution of the patent-in-suit, a series of references authored by Edward H. Reynolds ("Reynolds references"). Pl. Br. at 1. SKB avers that it is entitled to summary judgment on this issue because the "withheld" information is not material. During the 1960s and 1970s, Dr. Reynolds was part of a group that described a rare side effect in patients that were taking the then-marketed anti-epileptic drugs. Opening Expert Report of Edward H. Reynolds, MD, FRCP, FRCPsych, ("Reynolds Expert Report") ¶ 12, Attached to Declaration of Edward H. Reynolds, MD, FRCP, FRCPsych ("Reynolds Decl."). The pursuing studies revealed that many patients on these drugs exhibited folate deficiency without anemia. Id. The group's hypothesis was that the antifolate effects of these anticonvulsant drugs might be linked to their therapeutic, i.e. antiepileptic, action. Id. ¶ 13.

Alistair Miller, a named inventor of the '017 patent, relied on the Reynolds references when testing antifolate active drugs in the search for a new antiepileptic drug. Id. ¶ 14. Mr. Miller and his colleagues first tested two antifolate drugs already created by Wellcome⁵, pyrimethamine and trimethoprim, to determine if they had antiepileptic activity. Id. ¶ 16. After finding that both had such activity, Mr. Miller and Martin

⁵ Wellcome is a predecessor company to SKB.

Baxter, another named inventor of the '017 patent, conducted experimental studies in mice and confirmed that folic acid can cause convulsions. Id. ¶ 17. Thereafter, Mr. Miller investigated the antiepileptic activity of a series of pyrimidines and triazines, known antifolates, that had been first synthesized by Wellcome in the 1950s. Id. ¶ 18. The inventors observed that lamotrigine, a triazine, had antiepileptic activity and used it in the creation of the '017 patent. Id. ¶ 21. Despite its role as a starting point for the '017 inventors, the Reynolds references were not disclosed to the PTO. Teva claims that after considering the "totality of the circumstances", it is clear that the Reynolds references are material. Def. Opp'n at 11. SKB counters that the inventors used the Reynolds references only as a starting point for the '017 patent, and therefore it is not material prior art. Pl. Br. at 6.

The way in which an inventor is led to the invention is statutorily irrelevant to patentability. See 35 U.S.C. § 103(a) ("Patentability shall not be negated by the manner in which the invention was made."). Patentability is assessed from the perspective of the hypothetical person of ordinary skill in the art, therefore any information regarding the subjective motivations of individual inventors is not material. Life Techs. v. Clontech Labs., Inc., 224 F.3d 1320, 1325 (Fed. Cir. 2001) (citing Standard Oil Co. v. Am. Cyanimid Co., 774 F.2d 448, 454

(Fed. Cir. 1985)). Thus, the mere fact that SKB relied on the Reynolds references has no bearing on the issue of patentability. However, what is important is whether the Reynolds references, "in combination with other relevant prior art, would have rendered the claimed invention obvious to one of ordinary skill in the art; this inquiry, as a matter of law, is independent of the motivations that led the inventors to the claimed invention." Life Techs., at 1325. In support of its motion, SKB avers that all of the objective evidence indicates that a person of ordinary skill in the art would not have been motivated by the Reynolds hypothesis to make lamotrigine. Pl. Reply Br. at 3.

It is undisputed that in 1979, folate deficiency in humans was associated with a variety of side effects, including birth defects, neurological impairment and megaloblastic anemia. Pl. Statement of Material Facts ¶ 6-7; Def. Statement of Material Facts ¶ 6-7. Although the frequency of the occurrence of these side effects is in question⁶ it does not create an issue of fact for the Court as Teva does not dispute the possibility of serious side effects. SKB's expert, Dr. Ferrendelli concludes that

⁶ While SKB offers that compounds which had antifolate activity in humans were "known to cause serious side effects", Teva indicates that the document upon which SKB relies states that "the possibility of serious side-effects result[] from prolonged folate deficiency in patients." Id.; See Mental Effects of Anticonvulsants, and Folic Acid Metabolism, Attached to Rebuttal Expert Report of Professor James A. Ferrendelli, M.D., Ex. S at 205.

because of the side effects, a person of ordinary skill in the art would have been discouraged from investigating human antifolates as potential anticonvulsants. Rebuttal Expert Report of Professor James A. Ferrendelli, M.D., ¶ 33-35.

Furthermore, SKB avers that even if one had ignored the side effects caused by human antifolates, he would not have been motivated by the Reynolds hypothesis to test antimalarial⁷ phenyltriazines or to make lamotrigine. Pl. Reply at 4. It is undisputed that the Reynolds references do not mention phenyltriazines. Furthermore, SKB indicates that the Reynolds hypothesis was based on folate deficiency in humans. Id. In 1979, antimalarial phenyltriazines were only known to be antifolate in parasites and bacteria, not in humans. Id. Thus, a person of ordinary skill in the art would not have had a reasonable expectation that antimalarial phenyltriazines would have had human antifolate activity or that lamotrigine would be a potent anticonvulsant. Id. at 5. Dr. Rubin, SKB's malaria expert, has indicated that in 1977 "people were aware that antimalarials, which were also antifolates, had an effect on folate metabolism in humans." Def. Statement of Material Facts,

⁷ Malaria is an infectious disease caused by the presence of parasites in a host organism. Some antimalarial drugs disrupt the folate metabolism of the parasites, and thus exhibit "antifolic" or "antifolate" activity in that organism also. Rebuttal Expert Report of Professor Harvey Rubin, M.D., Ph.D., ¶ 15.

¶ 12. However, this does not alter the fact that it had no application to antimalarial phenyltriazines, the compound at issue. Moreover, it is undisputed that the '017 inventors "chose" to examine phenyltriazines because Wellcome had prior experience with these compounds in the 1950s. Pl. Reply at 5; Def. Opp'n at 1,4. Rather than provide evidence of how a person of ordinary skill in the art would have had a reasonable expectation to reach the same conclusions, Teva repeatedly argues that Dr. Reynolds' work was a motivating source for the '017 inventors. Def. Opp'n at 14-15. ("Dr. Reynolds's work did motivate the inventors to test the prior art compounds." Id. at 15.; . . .the inventors of the '017 patent relied on the Reynolds references . . . [c]learly this fact is relevant and indicates that the withheld art was material. Id. at 12.)).

In support of its motion, SKB also indicates that it is undisputed that even if one had been inclined to follow the Reynolds hypothesis, and had investigated known human antifolates, such as methotrexate, he would have discovered that methotrexate is not an anticonvulsant. Pl. Reply at 5. SKB adds that even if "one of ordinary skill had investigated phenyltriazines and screened them for human antifolate activity, and even if he had made and tested lamotrigine - none of which is suggested by Reynolds - he would have screened out lamotrigine because it has no appreciable human antifolate activity, and thus

would never have discovered its superior anticonvulsant properties." Pl. Reply at 6.

In its statement of material facts, Teva claims that SKB mischaracterizes the evidence and attempts to create an issue of fact by challenging SKB's findings. However, the Court finds that Teva's challenges do not create a genuine issue of material fact which contradict SKB's conclusion that lamotrigine has no appreciable human antifolate activity.⁸

2. The Rosenberg Paper

During prosecution of the '017 patent, the applicants cited to the patent examiner a document authored by Rosenberg and Bottirololi which "described a series of tests in which three antimalarial agents, quinacrine, chloroquine and hydroxychloroquine, were tested as anticonvulsants." See United States Patent No. 4,602,017 at 1-2, Attached to Declaration of Cedric C. Tan (Tan Decl.), Ex. A. Teva asserts that this article

⁸ For example, Teva argues that dihydrofolate reductase inhibition ("DHFR") is not the only model for human antifolate activity and therefore SKB's assertion that there was no link between antifolate activity and anticonvulsant activity is a misrepresentation of the evidence. Def. Opp'n at 20-21. This is not a misrepresentation because it is clear that the inventors were measuring lamotrigine's anticonvulsant activity based on mammalian DHFR inhibition. Additionally, Teva, in an attempt to prove intent to deceive, argues that this "misrepresentation" contradicts any evidence of good faith on the part of SKB. Def. Opp'n at 20. The Court does not find this argument persuasive either, as there is no valid evidence that the inventors did not believe, in good faith, that based on their research the Reynolds hypothesis was incorrect.

was "less relevant" than the Reynolds references. Reynolds Expert Report ¶ 11; Pl. Opp'n at 18. During prosecution of the patent, the examiner indicated that the article proved that there was a link between antimalarial activity and anticonvulsant activity. Tan Decl., Ex. L. at T 00711-715. Thus, the examiner maintained a position that because lamotrigine was in a class of compounds known to be antimalarials, it would have been obvious to use that class of compounds as an anticonvulsant. Id. In an amendment dated June 12, 1985, the applicants demonstrated that the Rosenberg antimalarials were structurally different and had dissimilar modes of action from the phenyltriazine antimalarials and thus the examiner's findings of obviousness were not accurate. Id. at T-00792-93.

Teva suggests that the inventors misled the PTO because they did not disclose the link between antifolates and anticonvulsant activity discussed in the Reynolds hypothesis. Teva proffers that Dr. Reynolds' work would have provided a basis for testing the phenyltriazines, including lamotrigine, for anticonvulsant activity because the phenyltriazines were known to be antifolates. Def. Opp'n at 7 n.5. For the reasons detailed above, the Court finds that one of ordinary skill in the art would not have found this as an adequate basis to conduct the testing.

Materiality is judged on the "overall degree of similarity

between the omitted reference and the claimed invention in light of the other prior art before the examiner." Baxter Int'l Inc. 149 F.3d at 1328. Teva has failed to meet its burden of proof. After reviewing the prior art in the record, the Court does not find that "there is a substantial likelihood that a reasonable examiner would consider it important in deciding whether to allow the application to issue as a patent." See 37 C.F.R. § 1.56(a) (1991). Accordingly, the Court determines that there are no genuine issues of material fact and based on the evidence presented, the threshold level of materiality has not been met.

*B. Intent to Deceive*⁹

The Court also concludes that Teva has failed to present evidence that SKB acted with an intent to deceive the PTO. The majority of Teva's arguments on this issue stem from its belief that the Court will infer an intent to deceive from its finding of materiality. Although intent to deceive the PTO may be inferred by the Court, even "gross negligence does not alone suffice to establish intent." CFMT, Inc. v. Yieldup Intern. Corp., 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing Kingsdown

⁹ Because the Court has already determined that the Reynolds references are not material, an in-depth analysis of the intent to deceive prong of the inequitable conduct test is unnecessary. Even though materiality and intent are balanced on a sliding scale, the Court must first find at least some evidence of materiality in order to proceed. See Pacific Furniture Mfg. Co. v. Preview Furniture Corp., 800 F.2d 1111, 1114 n.7 (Fed. Cir. 1986). However, in the interest of completeness, the Court will address the parties arguments on this matter.

Med. Consultants, Ltd. v. Hollister, Inc., 863 F.2d 867, 876 (Fed.Cir. 1988)). "Instead, 'the involved conduct, viewed in light of all the evidence, including evidence indicative of good faith, must indicate sufficient culpability to require a finding of intent to deceive'." Id. As with materiality, intent is a question of fact that must be proven by clear and convincing evidence. Dayco, 329 F.3d at 1362.

Teva claims that during prosecution of the '017 patent, applicants and their counsel withheld the Reynolds references while making assertions they could not have otherwise made had the Reynolds work been disclosed. Def. Opp'n at 16. These "assertions" are discussed more fully in Section A, supra. For the reasons cited above, the Court finds no merit in this argument and thus will not infer an intent to deceive from SKB's conduct.

Teva also urges the Court to draw intent from the fact that the inventors and related individuals cited to Reynolds' work before, during and after the '017 patent was prosecuted. Def. Opp'n at 17. In a 1994 article, Dr. Peck of the Wellcome Research Laboratories, stated that the Reynolds hypothesis was "seminal but erroneous." *Lamotrigine: Historical Background* at 96, Attached to Declaration of Christopher E. Loh, Ex. D ("The idea that folate inhibition was related to the mechanism of antiepileptic action was therefore seminal but erroneous, at

least for lamotrigine and related compounds with only weak activity against mammalian DHFR.").

"Intent to deceive cannot be inferred simply from the decision to withhold the reference where the reasons given for the withholding are plausible." Dayco, at 1367. The explanations given by SKB for withholding the Reynolds references, including the fact that it deemed the Reynolds hypothesis inaccurate, are not on their face implausible. The fact that the "inventors and related individuals" continued to cite to the Reynolds hypothesis has no bearing on a determination of materiality and thus cannot be used as evidence of intent to deceive. As such, the Court rejects Teva's attempt to infer intent to deceive from evidence that does not even support its argument for materiality. Accordingly, when drawing all factual inferences in its favor, the Court is convinced that Teva could not meet the clear and convincing standard of proof at trial. See Scripps Clinic & Research Foundation, 927 F.2d at 1583.

CONCLUSION

For the foregoing reasons, Plaintiff's motion for summary judgment of no inequitable conduct is granted.

/s/ John W. Bissell
JOHN W. BISSELL
Chief Judge
United States District Court

DATED: July 15, 2004